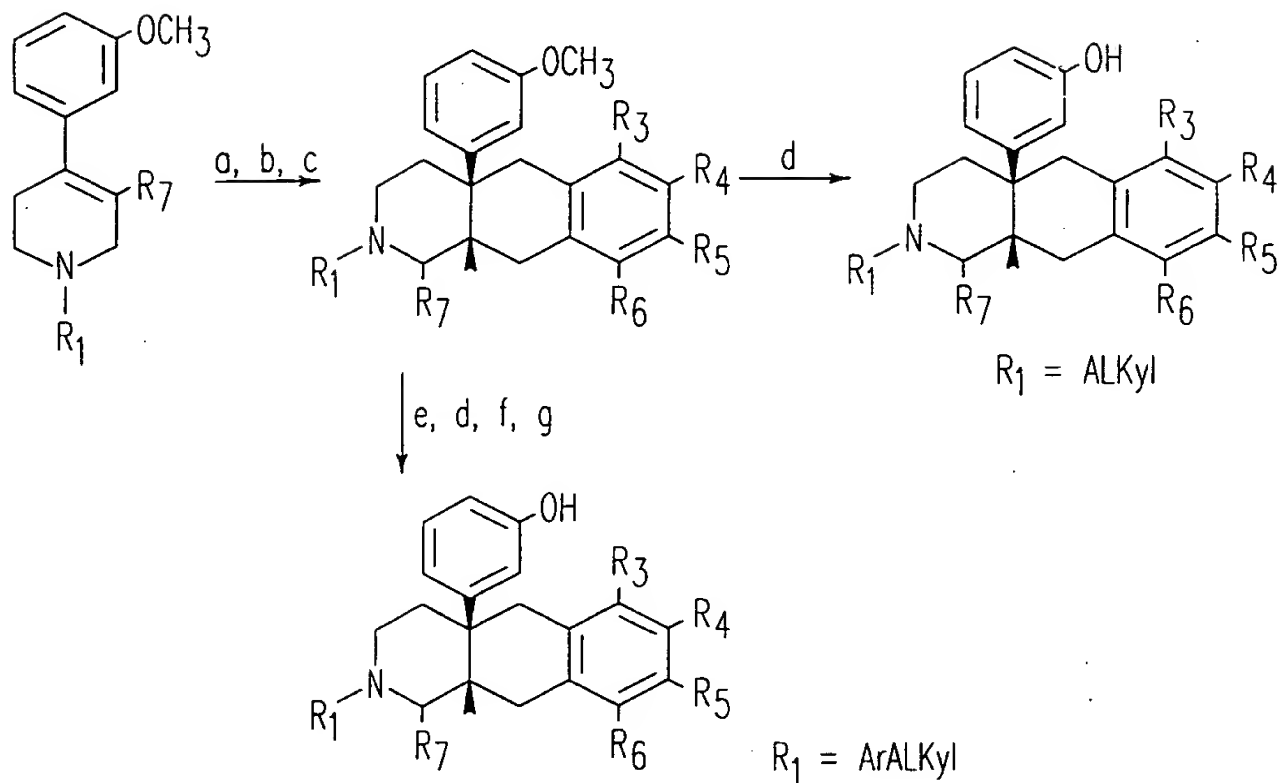
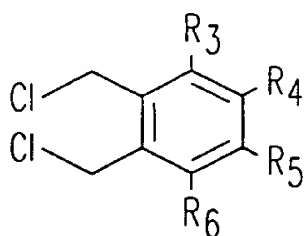


**FIG. 1**



Reagents: (a) *s*-BuLi, THF; AND



(b) NaI, CH<sub>3</sub>CN;

(c) NaBH<sub>4</sub>, EtOH;

(d) HBr, HOAc;

(e) PhOCOC<sub>2</sub>H<sub>5</sub>, toluene;

(f) aryl-alkyl-COOH, BOP, triethylamine, THF,

(g) borane/THF

FIG. 2A

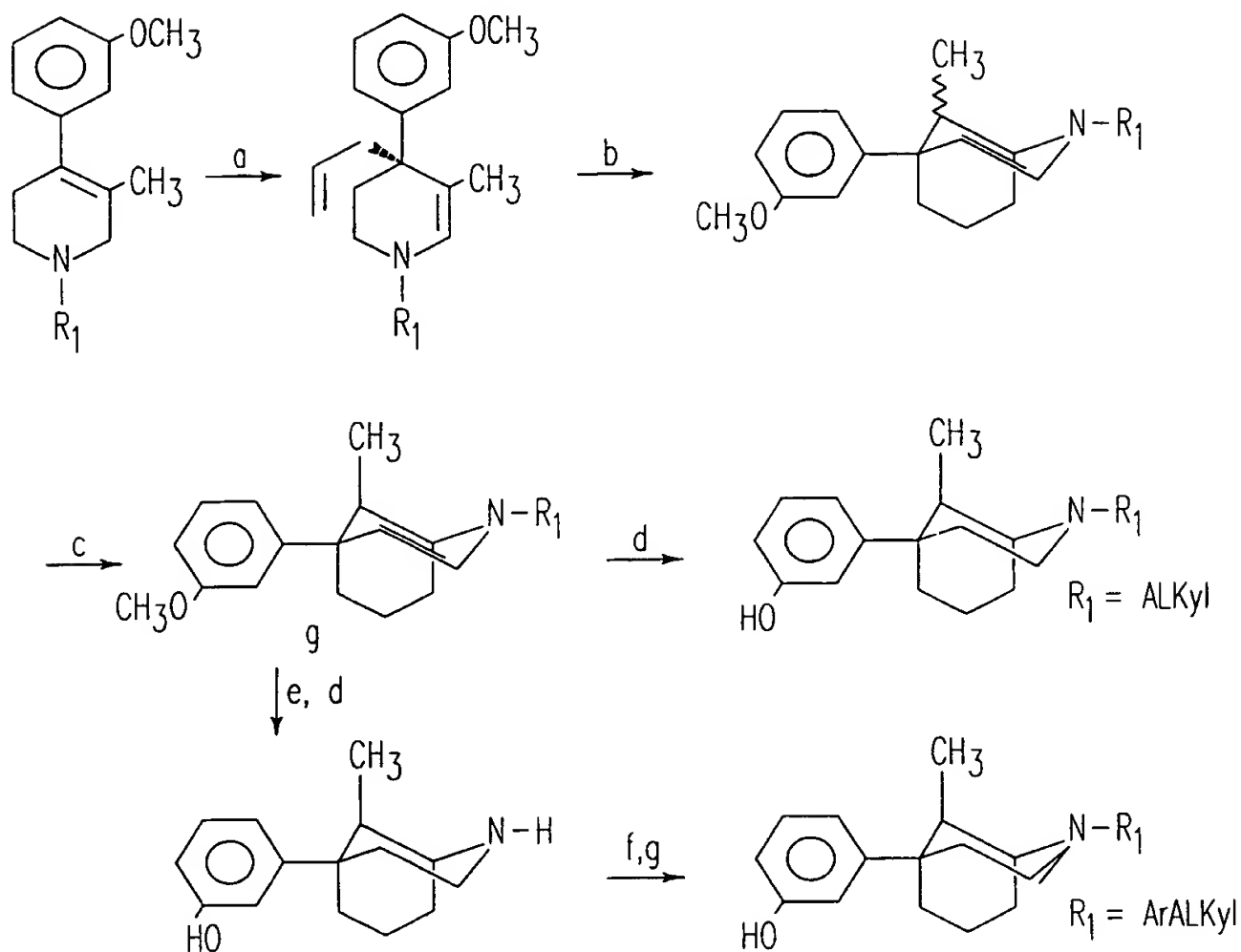
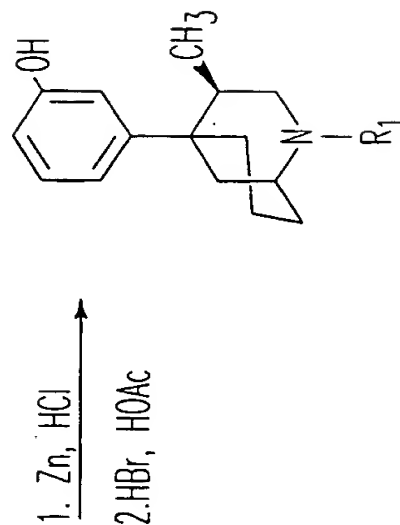
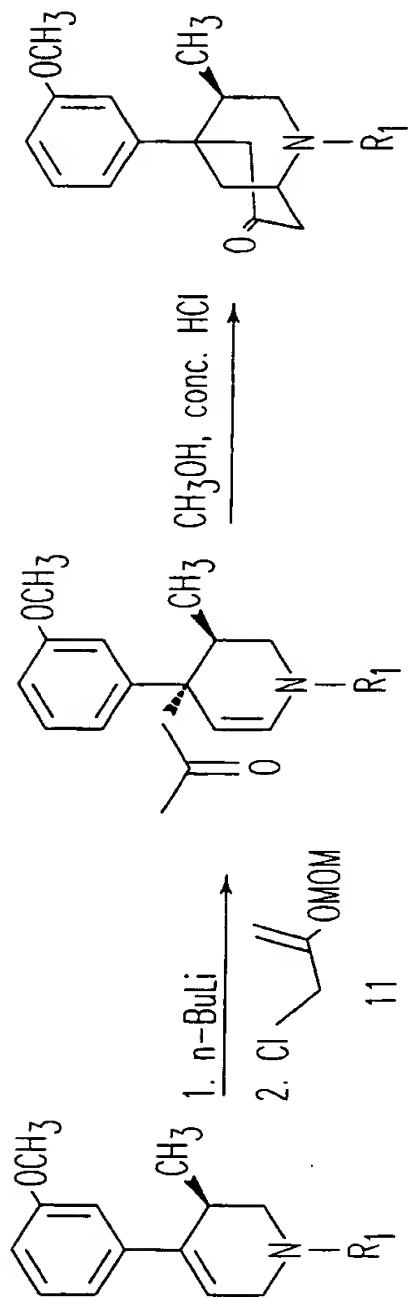


FIG. 2B



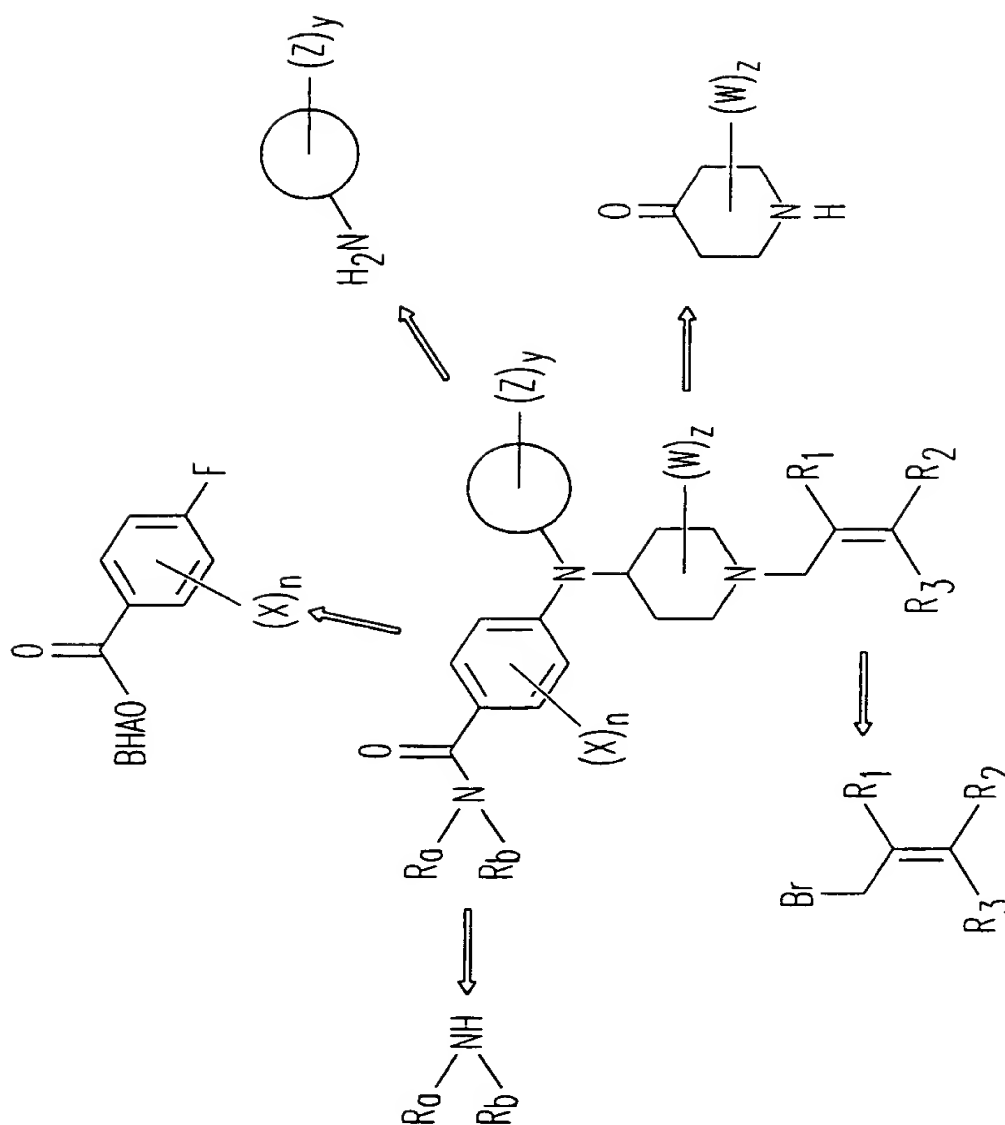
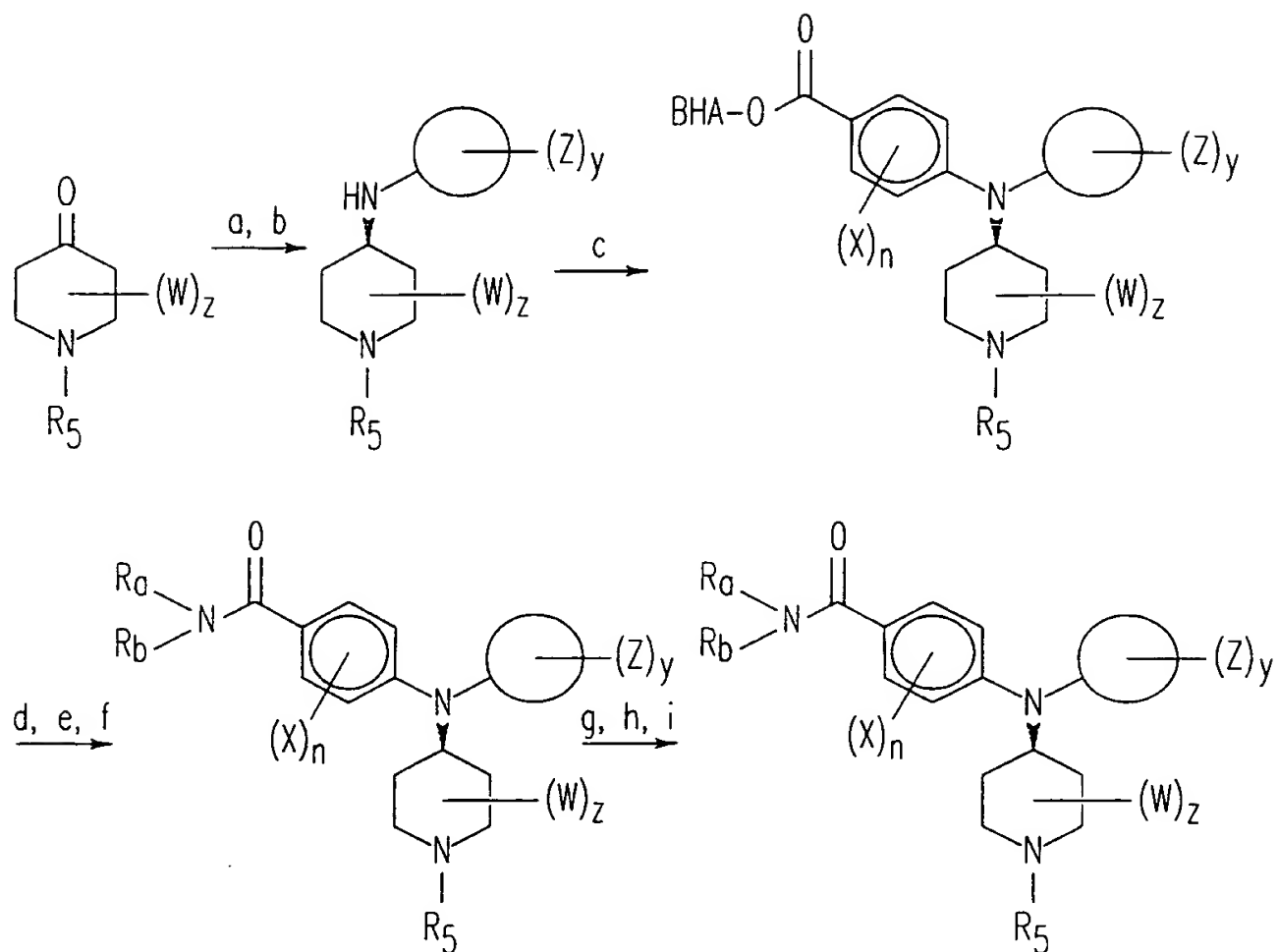
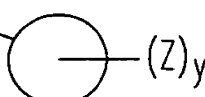


FIG. 3



FIG. 4



Reagents: (A)  $Ti(O-i-Pr)_4$ ,  $:NH$    $(Z)_y$

(b)  $NaBH_4$ , EtOH;

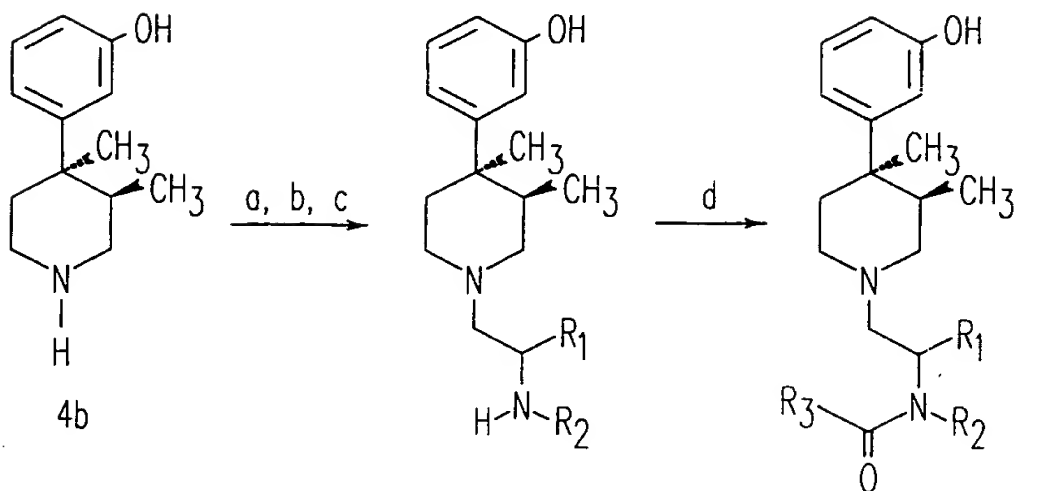
(c)  $n-BuLi$ , THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzoate;

(d) N-methylpyrrolidinone,  $NaOCH_3$ , toluene; (e) EtOH,  $H_2O$ ;

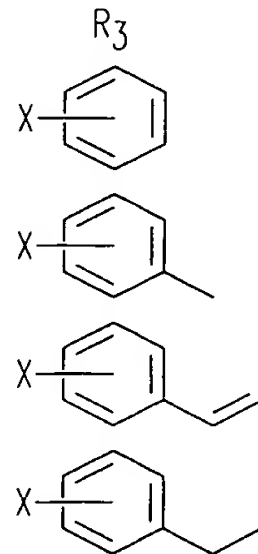
(f)  $R_aR_bNH$ , BOP,  $Et_3N$ ; (g)  $PhOCOCl$ ;

(h)  $KOH$ ,  $i-PrOH$ ,  $H_2O$ ; (i)  $R_5-Br$ , EtOH,  $K_2CO_3$

FIG. 5



|     | R <sub>1</sub>  | R <sub>2</sub>  |
|-----|-----------------|-----------------|
| 6a, | H               | H               |
| b,  | H               | CH <sub>3</sub> |
| c,  | CH <sub>3</sub> | H               |
| d,  | CH <sub>3</sub> | CH <sub>3</sub> |
| e,  | i-Pr            | H               |
| f,  | i-Pr            | H               |
| g,  | i-Bu            | H               |
| h,  | s-Bu            | H               |
| i,  | t-Hex           | H               |
| j,  | Ph              | CH <sub>3</sub> |
| k,  | Bn              | H               |



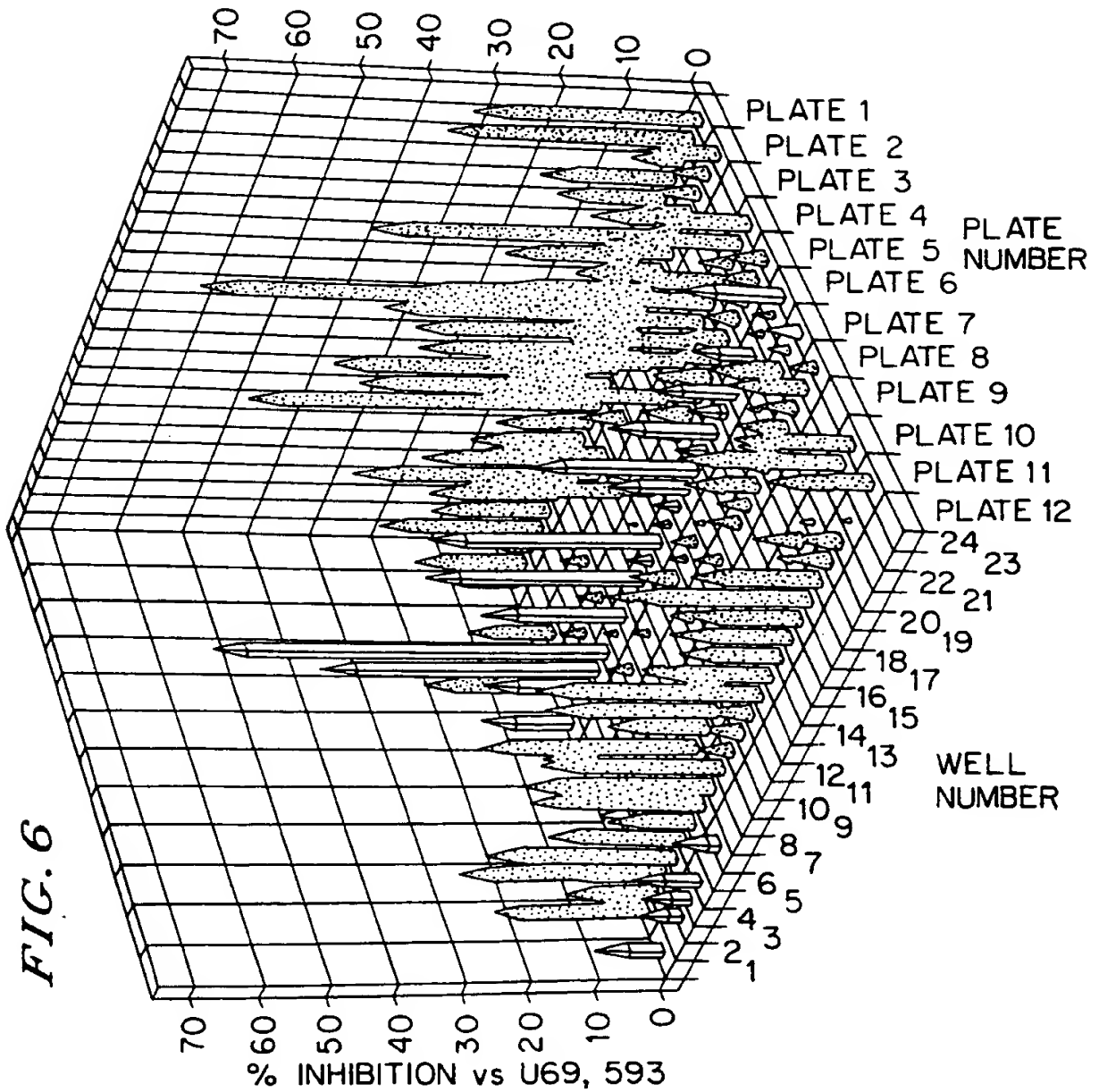
X=OH, OMe, OEt, OBn,  
 OnBu, OPh, Me, iPr, Bu,  
 Ph, NMe<sub>2</sub>, CONH<sub>2</sub>, F, Cl, Br.

<sup>a</sup> Reagents: (a) Boc-amino acid, BOP, TEA, THF;

(b) TFA, CH<sub>2</sub>Cl<sub>2</sub>;

(c) borane/dimethyl sulfide;

(d) R<sub>3</sub>CO<sub>2</sub>H, BOP, TEA, THF.



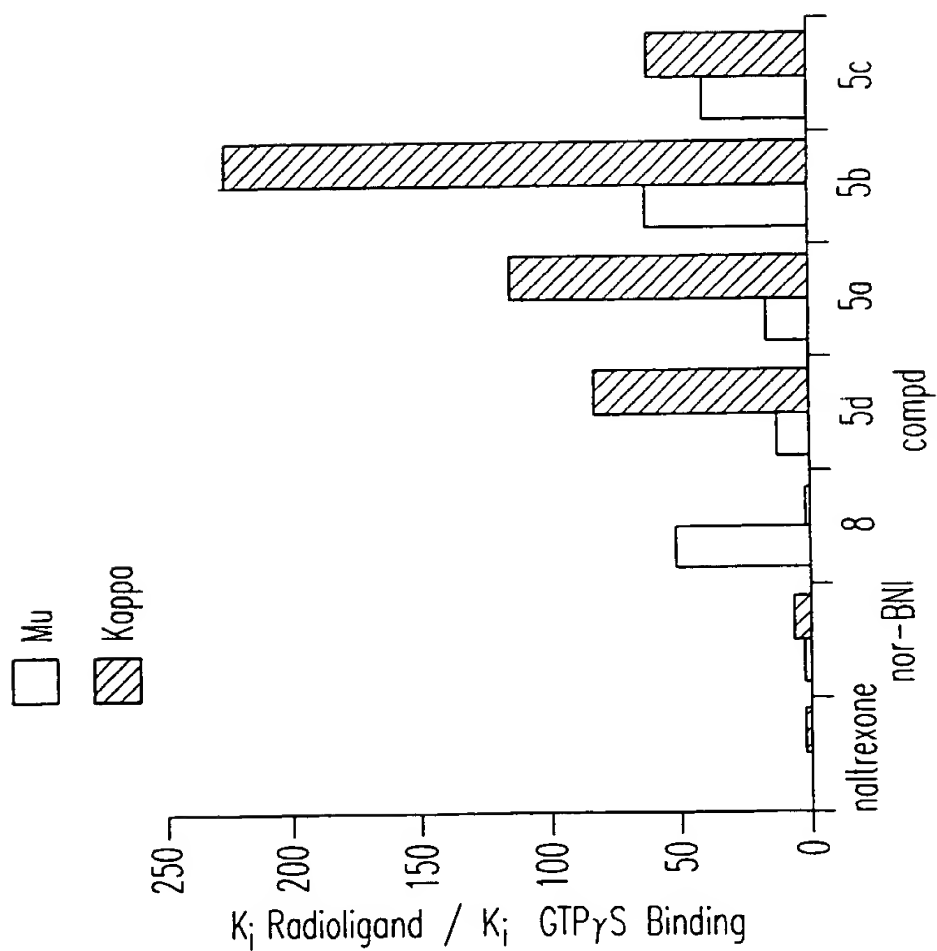
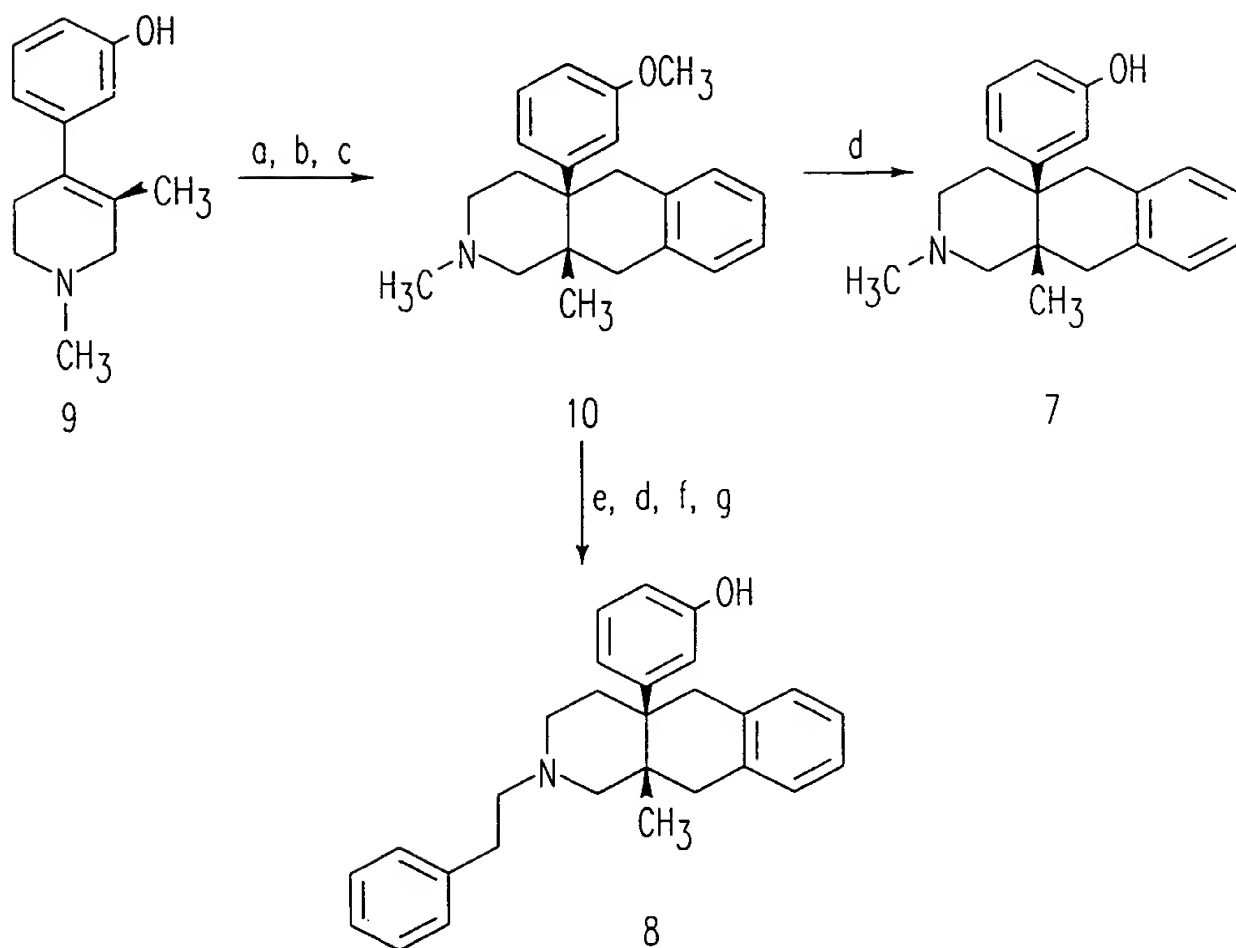


FIG. 7



**FIG. 8**



(a)  $s\text{-BuLi}$ , THF;  $\alpha,\alpha'$ -dichloroxylene;

(e)  $\text{PhOCOCi}$ , toluene;

(b)  $\text{NaI}$ ,  $\text{CH}_3\text{CN}$ ;

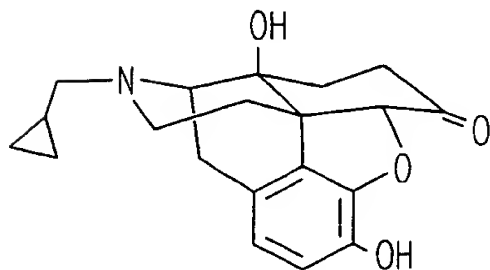
(f) Phenyl Acetic Acid, BOP, TEA, THF;

(c)  $\text{NaBH}_4$ , EtOH;

(g) Borane/THF;

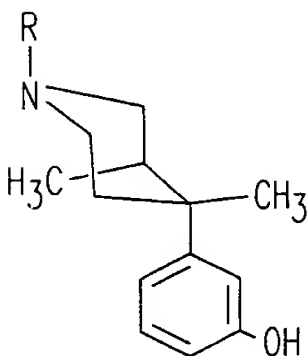
(d)  $\text{HBr}$ ,  $\text{HOAc}$ ;

**FIG. 9A**



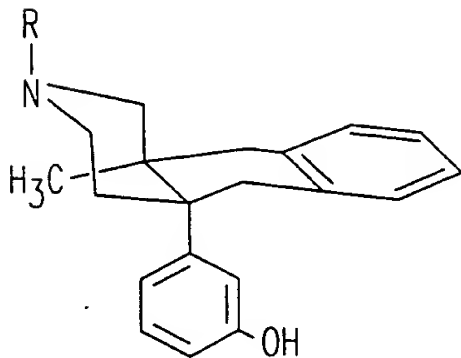
Naltrexone  
 (phenylaxial/piperidine chair)

**FIG. 9B**



3,4-Dimethyl-4-(3-hydroxyphenyl)piperidine  
 (phenylequatorial/piperidine chair)

**FIG. 9C**



8a-Methyl-4a-(3-hydroxyphenyl)octahydrobenzo[e]isoquinoline  
 (phenylequatorial/piperidine chair)

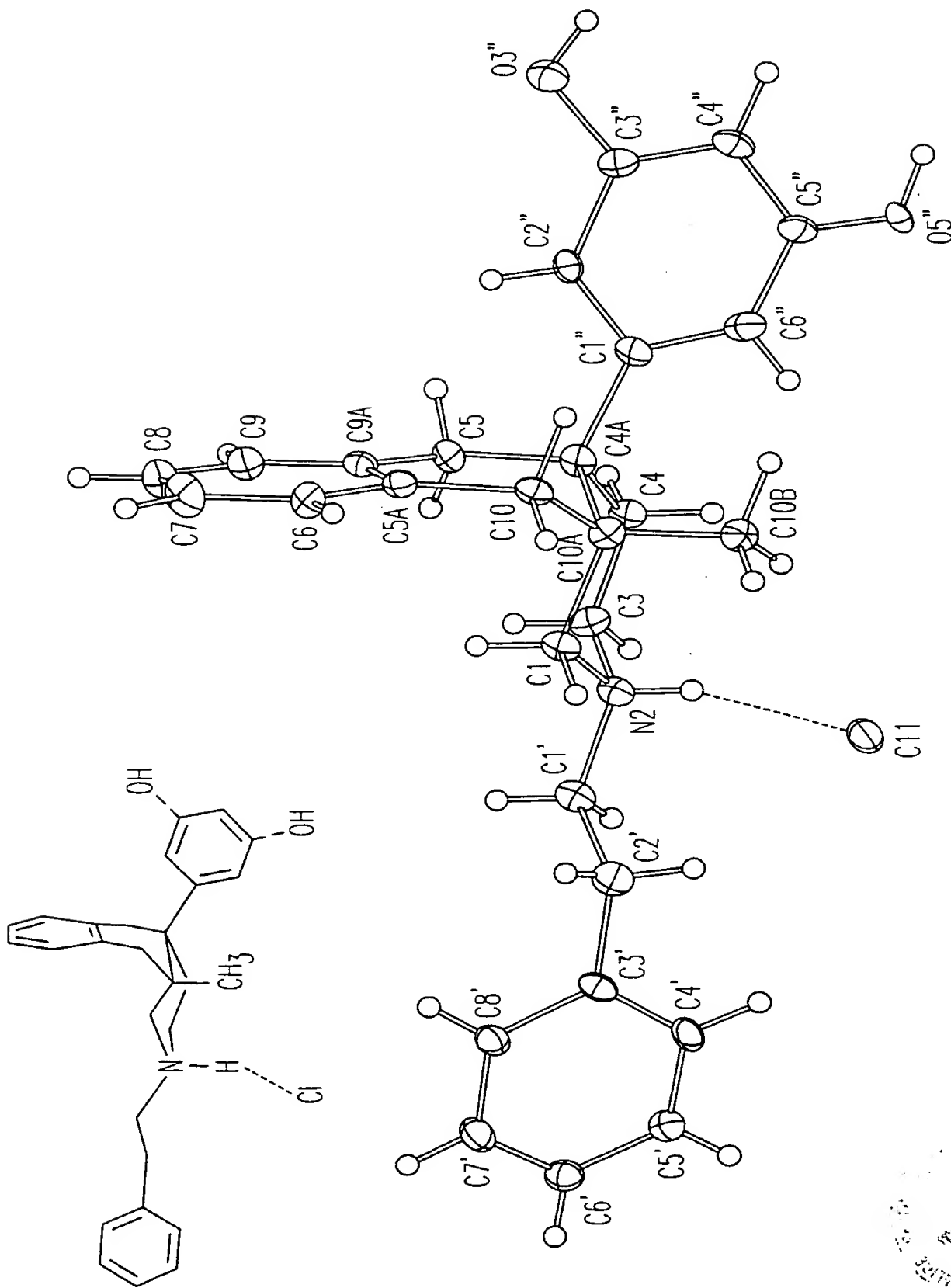


FIG. 10

FIG. 11

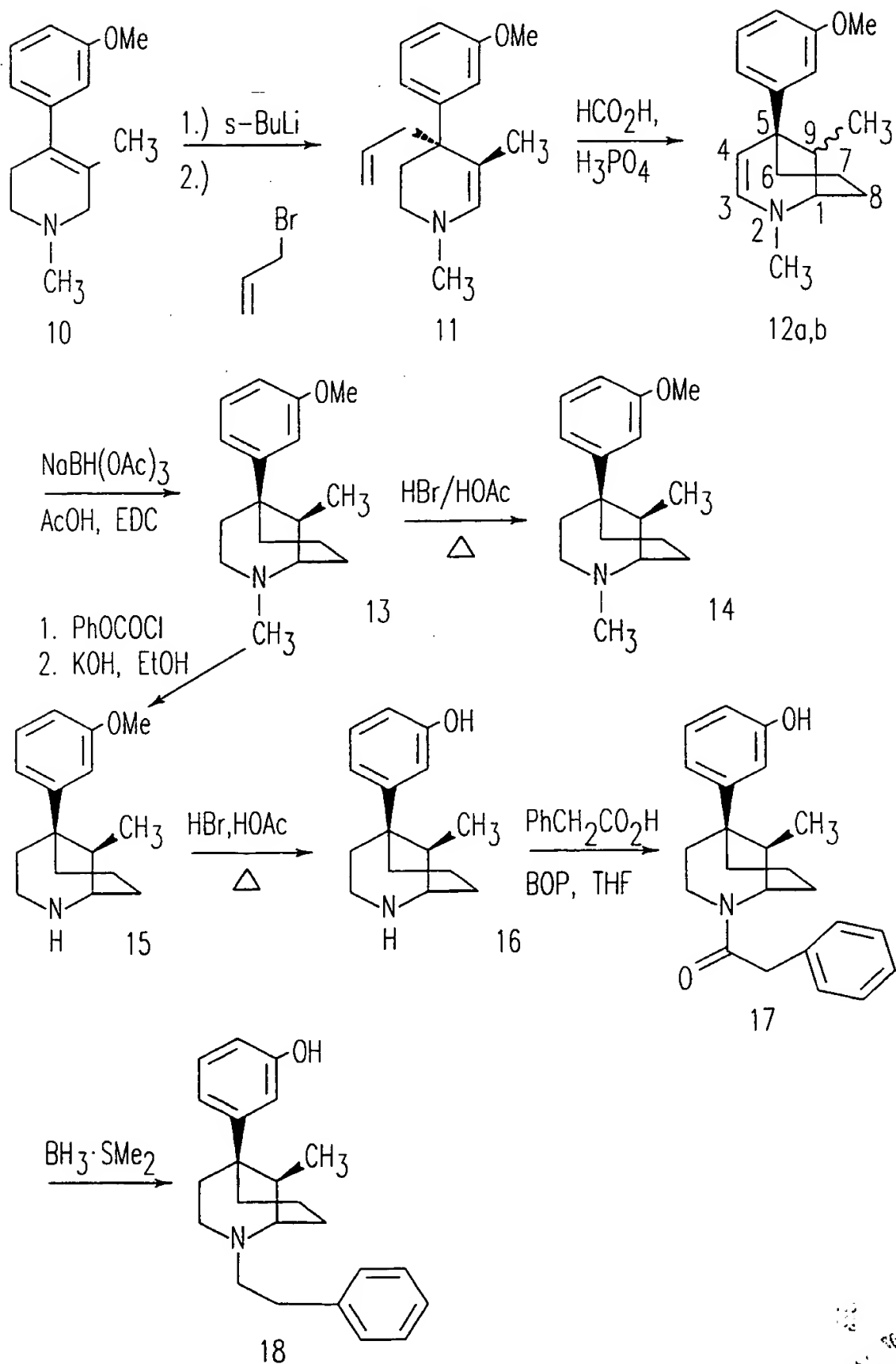


FIG. 12

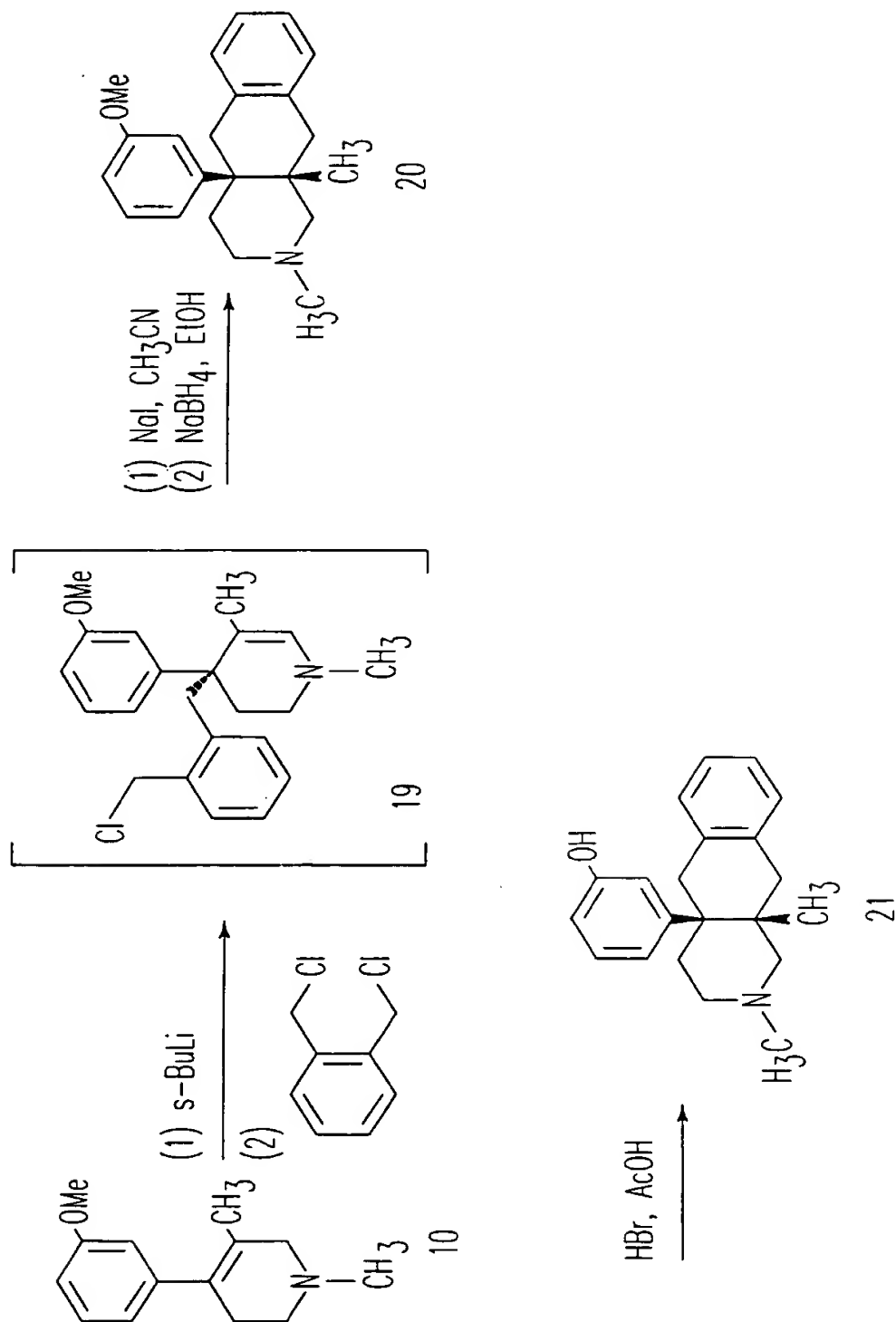
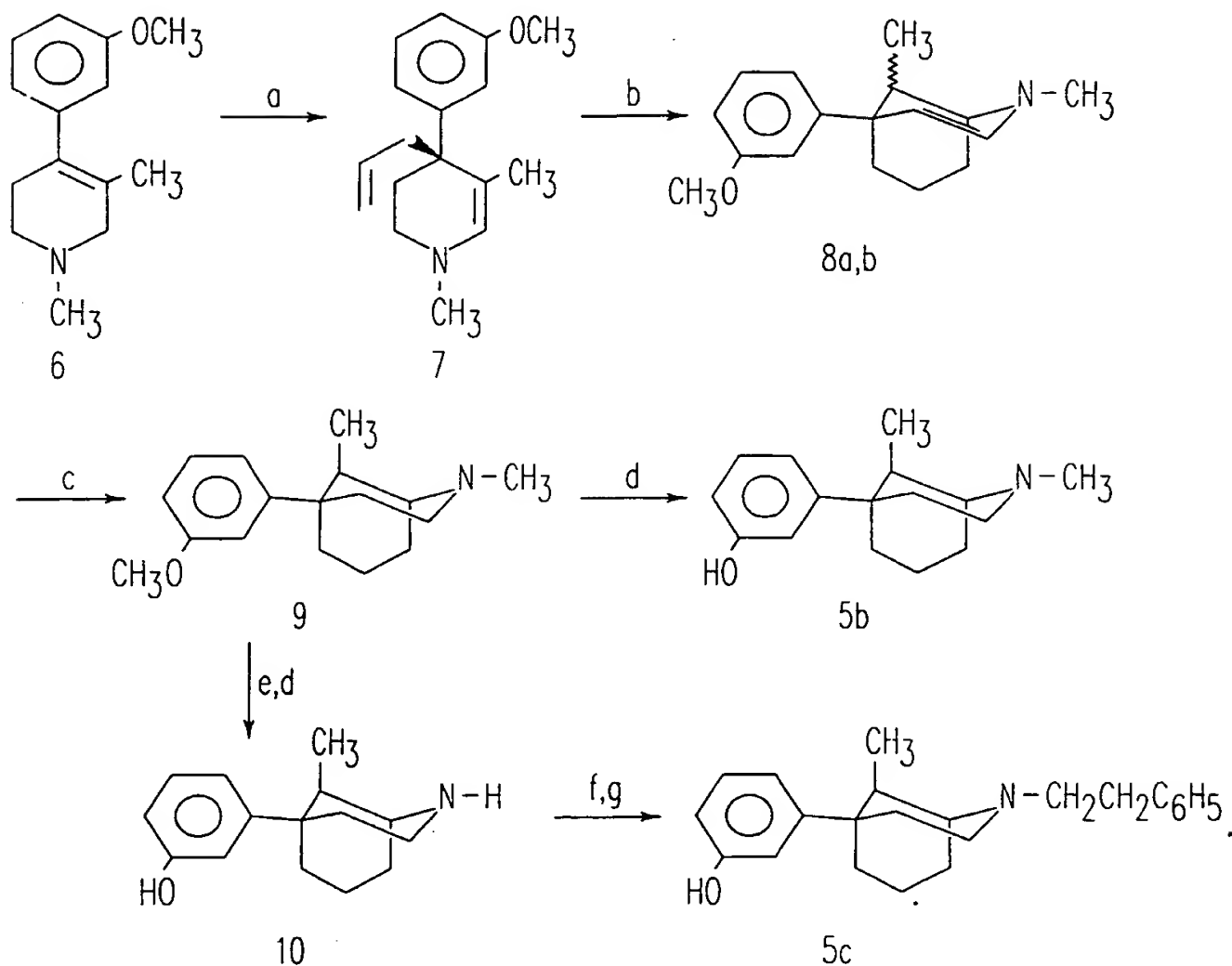


FIG. 13



<sup>a</sup> (a) *s*-BuLi, allyl-Br;

(b)  $H_3PO_4$ ,  $HCO_2H$ ;

(c)  $NaHB(OAc)_3$ ;

(d) HOAc, HBr;

(e)  $PhOCOCl$ , then KOH,  $H_2O$ ;

(f) (benzotriazol-1-yloxy)tris(dimethylamino)  
 phosphonium hexafluorophosphate,  $PhCH_2CO_2H$ ;

(g) borane-dimethyl sulfide, THF.

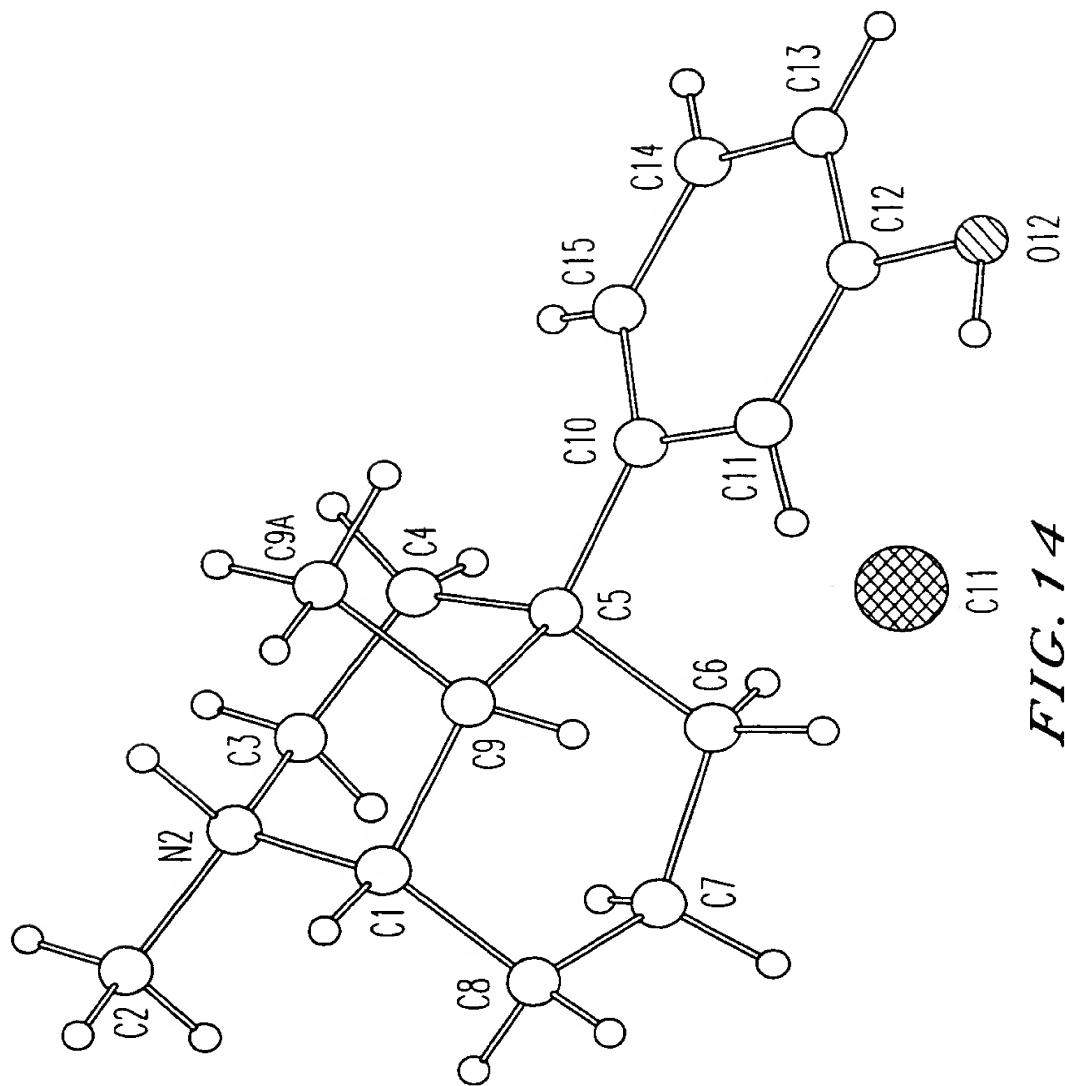
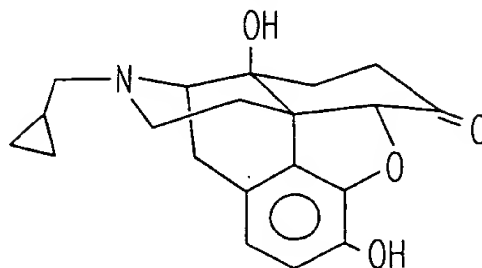


FIG. 14

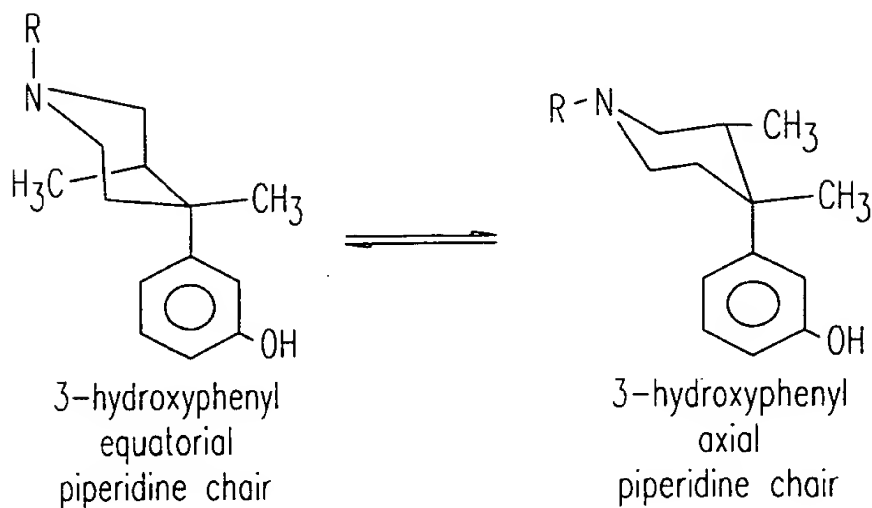
**FIG. 15**

Naltrexone (1b)

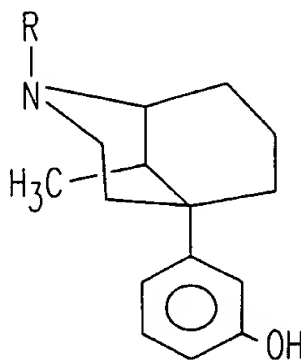


3-hydroxyphenyl axial piperidine chair

3,4-Dimethyl-4-(3-hydroxyphenyl)-piperidine (4)



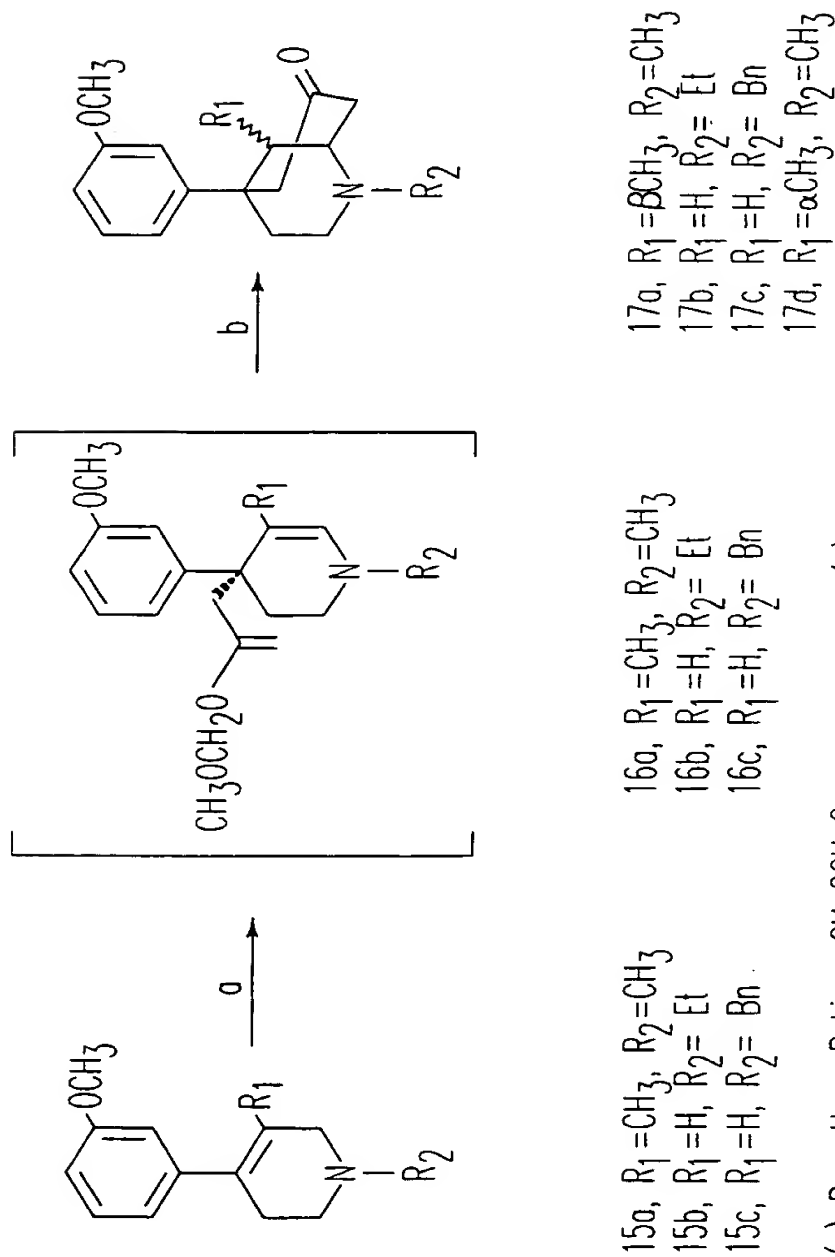
2-Alkyl-9 $\beta$ -methyl-5-(3-hydroxyphenyl)-  
morphan (5)



3-hydroxyphenyl equatorial piperidine chair



FIG. 16



(a)  $R_1 = H, n-BuLi$ ;  $CH_3OCH_2O$  (b)  $6N\ HCl, THF$

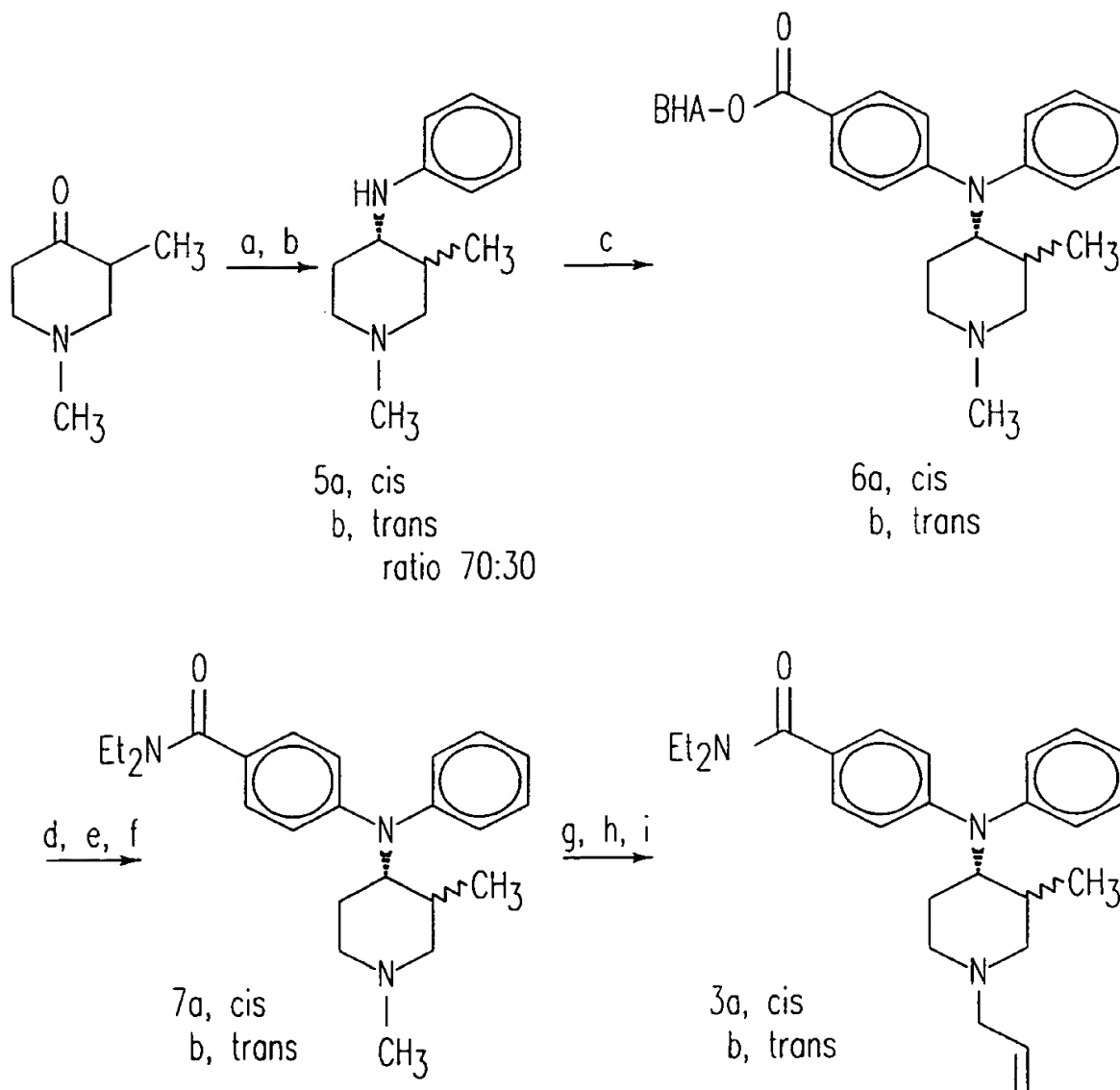
$R_1 = CH_3, s-BuLi$

TMEDA

18



FIG. 17



Reagents: (a)  $\text{Ti}(\text{O}-i\text{-Pr})_4$ , aniline; (b)  $\text{NaBH}_4$ , EtOH; (c)  $n\text{-BuLi}$ , THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzoate; (d) N-methylpyrrolidinone,  $\text{NaOCH}_3$ , toluene; (e) EtOH,  $\text{H}_2\text{O}$ ; (f)  $\text{Et}_2\text{NH}$ , BOP,  $\text{Et}_3\text{N}$ ; (g)  $\text{PhOCOCl}$ ; (h)  $\text{KOH}$ ,  $i\text{-PrOH}$ ,  $\text{H}_2\text{O}$ ; (i) allyl-Br, EtOH,  $\text{K}_2\text{CO}_3$

